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10/705,389	11/10/2003	Narayanan Sundararajan	21058/1206459-US2	4354
7278	7590	11/29/2007		
DARBY & DARBY P.C. P.O. BOX 770 Church Street Station New York, NY 10008-0770			EXAMINER SISSON, BRADLEY L	
			ART UNIT	PAPER NUMBER
			1634	
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			11/29/2007	PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

<b>Interview Summary</b>	<b>Application No.</b>	<b>Applicant(s)</b>	
	10/705,389	SUNDARARAJAN ET AL.	
	<b>Examiner</b>	<b>Art Unit</b>	
	Bradley L. Sisson	1634	

All participants (applicant, applicant's representative, PTO personnel):

(1) Bradley L. Sisson. (3)\_\_\_\_\_.

(2) Raj S. Dave', Reg. No. 42,465. (4)\_\_\_\_\_.

Date of Interview: 19 November 2007.

Type: a) ☒ Telephonic b) ☐ Video Conference  
c) ☐ Personal [copy given to: 1) ☐ applicant 2) ☐ applicant's representative]

Exhibit shown or demonstration conducted: d) ☒ Yes e) ☐ No.

If Yes, brief description: Draft response received via email ; copy attached.

Claim(s) discussed: 46-89, as presented in draft response.

Identification of prior art discussed: US Patent 6,280,939 B1 (Allen), US Patent 6,194,144 B1 (Koster), US Patent 6,635,452 B1 (Monforte et al.).

Agreement with respect to the claims f) ☒ was reached. g) ☐ was not reached. h) ☐ N/A.

Substance of Interview including description of the general nature of what was agreed to if an agreement was reached, or any other comments: See Continuation Sheet.

(A fuller description, if necessary, and a copy of the amendments which the examiner agreed would render the claims allowable, if available, must be attached. Also, where no copy of the amendments that would render the claims allowable is available, a summary thereof must be attached.)

THE FORMAL WRITTEN REPLY TO THE LAST OFFICE ACTION MUST INCLUDE THE SUBSTANCE OF THE INTERVIEW. (See MPEP Section 713.04). If a reply to the last Office action has already been filed, APPLICANT IS GIVEN A NON-EXTENDABLE PERIOD OF THE LONGER OF ONE MONTH OR THIRTY DAYS FROM THIS INTERVIEW DATE, OR THE MAILING DATE OF THIS INTERVIEW SUMMARY FORM, WHICHEVER IS LATER, TO FILE A STATEMENT OF THE SUBSTANCE OF THE INTERVIEW. See Summary of Record of Interview requirements on reverse side or on attached sheet.

Examiner Note: You must sign this form unless it is an Attachment to a signed Office action.

  
 Examiner's signature, if required

Continuation of Substance of Interview including description of the general nature of what was agreed to if an agreement was reached, or any other comments: Mr. Sisson indicated that the aspect of having a mass-modifying label present during the incorporation and detection phases of the method was evidence that the label was present during the method, but that it may not be present during all cycles of the assay. It was agreed that amending the claims so to reflect that the label is retained through a number of cycles would distinguish the invention over the prior art. Mr. Sisson noted that as presently worded, the method fairly encompasses sequencing a nucleic acid of virtually any length, and that paragraph 40 draws attention to a possible problem- that retention of the mass-modifying labels could create steric hindrance, and as a result, the labels may need to be removed after a point.

## Summary of Record of Interview Requirements

### Manual of Patent Examining Procedure (MPEP), Section 713.04, Substance of Interview Must be Made of Record

A complete written statement as to the substance of any face-to-face, video conference, or telephone interview with regard to an application must be made of record in the application whether or not an agreement with the examiner was reached at the interview

#### Title 37 Code of Federal Regulations (CFR) § 1.133 Interviews Paragraph (b)

In every instance where reconsideration is requested in view of an interview with an examiner, a complete written statement of the reasons presented at the interview as warranting favorable action must be filed by the applicant. An interview does not remove the necessity for reply to Office action as specified in §§ 1.111, 1.135. (35 U.S.C. 132)

#### 37 CFR §1.2 Business to be transacted in writing.

All business with the Patent or Trademark Office should be transacted in writing. The personal attendance of applicants or their attorneys or agents at the Patent and Trademark Office is unnecessary. The action of the Patent and Trademark Office will be based exclusively on the written record in the Office. No attention will be paid to any alleged oral promise, stipulation, or understanding in relation to which there is disagreement or doubt.

The action of the Patent and Trademark Office cannot be based exclusively on the written record in the Office if that record is itself incomplete through the failure to record the substance of interviews.

It is the responsibility of the applicant or the attorney or agent to make the substance of an interview of record in the application file, unless the examiner indicates he or she will do so. It is the examiner's responsibility to see that such a record is made and to correct material inaccuracies which bear directly on the question of patentability.

Examiners must complete an Interview Summary Form for each interview held where a matter of substance has been discussed during the interview by checking the appropriate boxes and filling in the blanks. Discussions regarding only procedural matters, directed solely to restriction requirements for which interview recordation is otherwise provided for in Section 812.01 of the Manual of Patent Examining Procedure, or pointing out typographical errors or unreadable script in Office actions or the like, are excluded from the interview recordation procedures below. Where the substance of an interview is completely recorded in an Examiners Amendment, no separate Interview Summary Record is required.

The Interview Summary Form shall be given an appropriate Paper No., placed in the right hand portion of the file, and listed on the "Contents" section of the file wrapper. In a personal interview, a duplicate of the Form is given to the applicant (or attorney or agent) at the conclusion of the interview. In the case of a telephone or video-conference interview, the copy is mailed to the applicant's correspondence address either with or prior to the next official communication. If additional correspondence from the examiner is not likely before an allowance or if other circumstances dictate, the Form should be mailed promptly after the interview rather than with the next official communication.

The Form provides for recordation of the following information:

- Application Number (Series Code and Serial Number)
- Name of applicant
- Name of examiner
- Date of interview
- Type of interview (telephonic, video-conference, or personal)
- Name of participant(s) (applicant, attorney or agent, examiner, other PTO personnel, etc.)
- An indication whether or not an exhibit was shown or a demonstration conducted
- An identification of the specific prior art discussed
- An indication whether an agreement was reached and if so, a description of the general nature of the agreement (may be by attachment of a copy of amendments or claims agreed as being allowable). Note: Agreement as to allowability is tentative and does not restrict further action by the examiner to the contrary.
- The signature of the examiner who conducted the interview (if Form is not an attachment to a signed Office action)

It is desirable that the examiner orally remind the applicant of his or her obligation to record the substance of the interview of each case. It should be noted, however, that the Interview Summary Form will not normally be considered a complete and proper recordation of the interview unless it includes, or is supplemented by the applicant or the examiner to include, all of the applicable items required below concerning the substance of the interview.

A complete and proper recordation of the substance of any interview should include at least the following applicable items:

- 1) A brief description of the nature of any exhibit shown or any demonstration conducted,
- 2) an identification of the claims discussed,
- 3) an identification of the specific prior art discussed,
- 4) an identification of the principal proposed amendments of a substantive nature discussed, unless these are already described on the Interview Summary Form completed by the Examiner,
- 5) a brief identification of the general thrust of the principal arguments presented to the examiner.  
(The identification of arguments need not be lengthy or elaborate. A verbatim or highly detailed description of the arguments is not required. The identification of the arguments is sufficient if the general nature or thrust of the principal arguments made to the examiner can be understood in the context of the application file. Of course, the applicant may desire to emphasize and fully describe those arguments which he or she feels were or might be persuasive to the examiner.)
- 6) a general indication of any other pertinent matters discussed, and
- 7) if appropriate, the general results or outcome of the interview unless already described in the Interview Summary Form completed by the examiner.

Examiners are expected to carefully review the applicant's record of the substance of an interview. If the record is not complete and accurate, the examiner will give the applicant an extendable one month time period to correct the record.

#### Examiner to Check for Accuracy

If the claims are allowable for other reasons of record, the examiner should send a letter setting forth the examiner's version of the statement attributed to him or her. If the record is complete and accurate, the examiner should place the indication, "Interview Record OK" on the paper recording the substance of the interview along with the date and the examiner's initials.

**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

Examiner: B. L. Sisson

**AMENDMENTS TO THE CLAIMS****Listing of Claims:**

This Listing of Claims will replace all prior versions, and listings, of claims in the application:

1-45 (Cancelled)

46. (Currently amended) A method for sequencing nucleic acid, comprising:

a) attaching a template nucleic acid molecule having from about 10 to approximately 100,000 nucleotides in length to a cantilever suitable for detecting a mass dependent property associated with the cantilever, resulting in forming an attached template nucleic acid; wherein the attached template nucleic acid is partially double stranded prior to, concurrent with or subsequent to the attaching of the template nucleic acid;

b) contacting the attached template nucleic acid molecule with at least one type of a complimentary nucleotide structurally suitable for mass labeling; wherein the complimentary nucleotide comprises a 3' blocking or protecting group;

c) incubating the attached template nucleic acid molecule and the complimentary nucleotide under conditions suitable for incorporating the complimentary nucleotide to the attached template nucleic acid in a position complementary to a nucleotide in the attached template nucleic acid, wherein the complimentary nucleotide incorporated in the attached template nucleic acid is mass labeled prior to, concurrent with, or subsequent to the incorporation, yet prior to the addition of a next complimentary nucleotide; wherein complimentary nucleotides of different types have different mass labels that are attached to the complimentary nucleotides during said method for

sequencing nucleic acid; and

d) identifying the complimentary nucleotide incorporated in the attached template nucleic acid by detecting a change in the mass dependent property associated with the cantilever, wherein the change is indicative of the incorporation of the complimentary nucleotide in the attached template nucleic acid.

47. (Original) The method of claim 46, wherein the complimentary nucleotide comprises a chemical structure selected from the group consisting of deoxyadenosine 5' triphosphate (dATP), deoxythymidine 5' triphosphate (dTTP), deoxyguanosine 5' triphosphate (dGTP) and deoxycytosine 5' triphosphate (dCTP).

48. (Original) The method of claim 46, wherein the complimentary nucleotide comprises a chemical structure selected from the group consisting of adenosine 5' triphosphate (ATP), thymidine 5' triphosphate (TTP), guanosine 5' triphosphate (GTP) and cytosine 5' triphosphate (CTP).

49. (Original) The method of claim 46, wherein the change in the mass dependent property of the structure is determined by detecting deflection and/or resonant frequency shifts in the cantilever.

50. (Original) The method of claim 49, wherein the deflection and/or resonant frequency

51. (Original) The method of claim 46, wherein a single nucleotide polymorphism (SNP) is identified.

52. (Original) The method of claim 46, further comprising iteratively repeating parts b) through d), wherein for each iteration the attached template is contacted with a different type of complimentary nucleotide.

53. (Original) The method of claim 46, further comprising hybridizing a primer to the attached template nucleic acid.

54. (Original) The method of claim 53, wherein the labeled nucleotides are covalently attached to the 3' end of the primer by a polymerase.

55. (Original) The method of claim 46, wherein the method comprises a plurality of cantilevers, the cantilevers being arranged in a selected pattern.

56. (Original) A method for sequencing nucleic acid, comprising:

a) attaching a template nucleic acid molecule having from about 10 to approximately 100,000 nucleotides in length to a cantilever suitable for detecting a mass dependent property



associated with the cantilever, resulting in forming an attached template nucleic acid; wherein the attached template nucleic acid is partially double stranded prior to, concurrent with or subsequent to the attaching of the template nucleic acid;

b) contacting the attached template nucleic acid molecule with a first type of complimentary nucleotide structurally suitable for mass labeling, a second type of complimentary nucleotide structurally suitable for mass labeling, a third type of complimentary nucleotide structurally suitable for mass labeling, and a fourth type of complimentary nucleotide structurally suitable for mass labeling; wherein the first, second, third and fourth types of complimentary nucleotides comprise a 3' blocking or protecting group;

c) incubating the attached template nucleic acid molecule and the first, second, third and fourth types of complimentary nucleotides under conditions suitable for incorporating the first type of complimentary nucleotide to the attached template nucleic acid in a position complementary to a nucleotide in the attached template nucleic acid, wherein the first type of complimentary nucleotide incorporated in the attached template nucleic acid is mass labeled prior to, concurrent with, or subsequent to the incorporation, yet prior to the addition of a next complimentary nucleotide; wherein the first, second, third and fourth types of complimentary nucleotides have different mass labels that are attached to the complimentary nucleotides during said method for sequencing nucleic acid; and

d) identifying the first type of complimentary nucleotide incorporated in the attached template nucleic acid by detecting a change in the mass dependent property associated with the cantilever, wherein the change is indicative of the incorporation of the first type of complimentary

nucleotide in the attached template nucleic acid.

57. (Original) The method of claim 56, wherein one or more of the first, second, third and fourth types of complimentary nucleotides comprise a chemical structure selected from the group consisting of deoxyadenosine 5' triphosphate (dATP), deoxythymidine 5' triphosphate (dTTP), deoxyguanosine 5' triphosphate (dGTP) and deoxycytosine 5' triphosphate (dCTP).

58. (Original) The method of claim 56, wherein one or more of the first, second, third and fourth types of complimentary nucleotides comprise a chemical structure selected from the group consisting of adenosine 5' triphosphate (ATP), thymidine 5' triphosphate (TTP), guanosine 5' triphosphate (GTP) and cytosine 5' triphosphate (CTP).

59. (Original) The method of claim 56, wherein the change in the mass dependent property of the structure is determined by detecting deflection and/or resonant frequency shifts in the cantilever.

60. (Original) The method of claim 59, wherein the deflection and/or resonant frequency shift is detected by optical beam detection, piezoelectric detection, piezoresistance detection or electrical resistance detection.

61. (Original) The method of claim 56, wherein a single nucleotide polymorphism (SNP) is identified.

63. (Original) The method of claim 56, further comprising hybridizing a primer to the attached template nucleic acid.

64. (Original) The method of claim 63, wherein the labeled nucleotides are covalently attached to the 3' end of the primer by a polymerase.

65. (Original) The method of claim 56, wherein the method comprises a plurality of cantilevers, the cantilevers being arranged in a selected pattern.

66. (Original) A method for sequencing nucleic acid, comprising:

a) attaching a template nucleic acid molecule having from about 10 to approximately 100,000 nucleotides in length to a cantilever suitable for detecting a mass dependent property associated with the cantilever, resulting in forming an attached template nucleic acid; wherein the attached template nucleic acid is partially double stranded prior to, concurrent with or subsequent to the attaching of the template nucleic acid;

b) contacting the attached template nucleic acid molecule of a) with at least one type of a complimentary nucleotide structurally suitable for mass labeling; wherein the complimentary nucleotide optionally comprises a 3' blocking or protecting group;

c) incubating the attached template nucleic acid molecule and the complimentary nucleotide under conditions suitable for incorporating the complimentary nucleotide to the attached template nucleic acid in a position complementary to a nucleotide in the attached template nucleic acid, wherein the complimentary nucleotide incorporated in the attached template nucleic acid is mass labeled prior to, or concurrent with the incorporation, yet prior to the addition of a next complimentary nucleotide; wherein complimentary nucleotides of different types have different mass labels that are attached to the complimentary nucleotides during said method for sequencing nucleic acid; and

d) identifying the complimentary nucleotide incorporated in the attached template nucleic acid by detecting a change in the mass dependent property associated with the cantilever, wherein the change is indicative of the incorporation of the complimentary nucleotide in the attached template nucleic acid.

67. (Original) The method of claim 66, wherein the complimentary nucleotide comprises a chemical structure selected from the group consisting of deoxyadenosine 5' triphosphate (dATP), deoxythymidine 5' triphosphate (dTTP), deoxyguanosine 5' triphosphate (dGTP) and deoxycytosine 5' triphosphate (dCTP).

68. (Original) The method of claim 66, wherein the complimentary nucleotide comprises a chemical structure selected from the group consisting of adenosine 5' triphosphate (ATP), thymidine 5' triphosphate (TTP), guanosine 5' triphosphate (GTP) and cytosine 5' triphosphate (CTP).

69. (Original) The method of claim 66, wherein the change in the mass dependent property of the structure is determined by detecting deflection and/or resonant frequency shifts in the cantilever.

70. (Original) The method of claim 69, wherein the deflection and/or resonant frequency shift is detected by optical beam detection, piezoelectric detection, piezoresistance detection or electrical resistance detection.

71. (Original) The method of claim 66, wherein a single nucleotide polymorphism (SNP) is identified.

72. (Original) The method of claim 66, further comprising iteratively repeating parts b) through d), wherein for each iteration the attached template is contacted with a different type of complimentary nucleotide.

73. (Original) The method of claim 66, further comprising hybridizing a primer to the attached template nucleic acid.

74. (Original) The method of claim 73, wherein the labeled nucleotides are covalently attached to the 3' end of the primer by a polymerase.

75. (Original) The method of claim 66, wherein the method comprises a plurality of

cantilevers, the cantilevers being arranged in a selected pattern.

76. (Original) A method for sequencing nucleic acid, comprising:

a) attaching a template nucleic acid molecule having from about 10 to approximately 100,000 nucleotides in length to a cantilever suitable for detecting a mass dependent property associated with the cantilever, resulting in forming an attached template nucleic acid; wherein the attached template nucleic acid is partially double stranded prior to, concurrent with or subsequent to the attaching of the template nucleic acid;

b) contacting the attached template nucleic acid molecule with a first type of complimentary nucleotide structurally suitable for mass labeling, a second type of complimentary nucleotide structurally suitable for mass labeling, a third type of complimentary nucleotide structurally suitable for mass labeling, and a fourth type of complimentary nucleotide structurally suitable for mass labeling; wherein the first, second, third and fourth types of complimentary nucleotides optionally comprise a 3' blocking or protecting group;

c) incubating the attached template nucleic acid molecule and the first, second, third and fourth types of complimentary nucleotides under conditions suitable for incorporating the first type of complimentary nucleotide to the attached template nucleic acid in a position complementary to a nucleotide in the attached template nucleic acid, wherein the first type of complimentary nucleotide incorporated in the attached template nucleic acid is mass labeled prior to, or concurrent with the incorporation, yet prior to the addition of a next complimentary nucleotide; wherein the first, second, third and fourth types of complimentary nucleotides have

different mass labels that are attached to the complimentary nucleotides during said method for sequencing nucleic acid; and

d) identifying the first type of complimentary nucleotide incorporated in the attached template nucleic acid by detecting a change in the mass dependent property associated with the cantilever, wherein the change is indicative of the incorporation of the first type of complimentary nucleotide in the attached template nucleic acid.

77. (Original) The method of claim 76, wherein one or more of the first, second, third and fourth types of complimentary nucleotides comprise a chemical structure selected from the group consisting of deoxyadenosine 5' triphosphate (dATP), deoxythymidine 5' triphosphate (dTTP), deoxyguanosine 5' triphosphate (dGTP) and deoxycytosine 5' triphosphate (dCTP).

78. (Original) The method of claim 76, wherein one or more of the first, second, third and fourth types of complimentary nucleotides comprise a chemical structure selected from the group consisting of adenosine 5' triphosphate (ATP), thymidine 5' triphosphate (TTP), guanosine 5' triphosphate (GTP) and cytosine 5' triphosphate (CTP).

79. (Original) The method of claim 76, wherein the change in the mass dependent property of the structure is determined by detecting deflection and/or resonant frequency shifts in the cantilever.

80. (Original) The method of claim 79, wherein the deflection and/or resonant frequency shift is detected by optical beam detection, piezoelectric detection, piezoresistance detection or electrical resistance detection.

81. (Original) The method of claim 76, wherein a single nucleotide polymorphism (SNP) is identified.

82. (Original) The method of claim 76, further comprising iteratively repeating parts b) through d), wherein for each iteration the attached template is contacted with a different type of complimentary nucleotide.

83. (Original) The method of claim 76, further comprising hybridizing a primer to the attached template nucleic acid.

84. (Original) The method of claim 83, wherein the labeled nucleotides are covalently attached to the 3' end of the primer by a polymerase.

85. (Original) The method of claim 76, wherein the method comprises a plurality of cantilevers, the cantilevers being arranged in a selected pattern.

86. (New) The method of claim 46, wherein the mass labels are selected from the group consisting of nanoparticles, nanoparticle aggregates, carbon nanotubes, fullerenes, functionalized



87. (New) The method of claim 56, wherein the mass labels are selected from the group consisting of nanoparticles, nanoparticle aggregates, carbon nanotubes, fullerenes, functionalized fullerenes, functionalized fullerenes, quantum dots, dendrimers, polymers, and combinations thereof.

88. (New) The method of claim 66, wherein the mass labels are selected from the group consisting of nanoparticles, nanoparticle aggregates, carbon nanotubes, fullerenes, functionalized fullerenes, functionalized fullerenes, quantum dots, dendrimers, polymers, and combinations thereof.

89. (New) The method of claim 76, wherein the mass labels are selected from the group consisting of nanoparticles, nanoparticle aggregates, carbon nanotubes, fullerenes, functionalized fullerenes, functionalized fullerenes, quantum dots, dendrimers, polymers, and combinations thereof.

**REMARKS**

The undersigned thanks Examiner Sisson for withdrawing the rejections in the Action of April 23, 2007.

Independent claims 46, 56, 66 and 76 have been amended to recite that “complimentary nucleotides have different mass labels that are attached to the complimentary nucleotides during said method for sequencing nucleic acid.” This underlined limitation is supported by paragraph [0035] of the specification which states that “[t]he identity of an incorporated labeled nucleotide 218 may be determined from the distinctive change in mass and/or surface stress of the structure 116, 212.” This statement means that the mass labels are attached to the complimentary nucleotides during the method for sequencing nucleic acid in order for the identity of an incorporated labeled nucleotide 218 be determined from the distinctive change in mass and/or surface stress of the structure 116, 212.

**Claim Rejections - 35 USC 103**

Claims 46-85 were rejected as being obvious over Allen in view of Köster and Monforte. This rejection is respectfully traversed.

The Examiner acknowledges that Allen fails to teach mass labels or the use of 3' blocking groups. See paragraph 8 of the Action. The Examiner attempts to fill these gaps in Allen by resorting to Köster and Monforte. However, both Köster and Monforte relate to releasable mass labels that are *released during the DNA sequencing*. On the other hand, in the method of the claimed invention the *mass labels are attached to the complimentary nucleotides during said method for sequencing nucleic acid* as recited in independent claims 46, 56, 66 and 76.

Furthermore, the DNA sequencing methods of Allen and the present invention are totally different from those of Köster and Monforte. The DNA sequencing methods of Allen and the present invention rely on a *cantilever method* to detect increment of mass by the addition of a nucleotide. On the other hand, the methods of Köster and Monfort rely on *mass spectroscopy* wherein a mass label is released during DNA sequencing for the determination of a DNA sequence. The cantilever method of Allen and the mass spectroscopy methods of Köster and Monfort operate on totally different mechanisms. In the cantilever method of Allen, the identity of a nucleotide is determined by “a local sensitive force detector capable of reliably detecting the incorporation of a nucleotide of interest into a growing polynucleotide chain.” See column 4, lines 24-27, of Allen. On the other hand, in the mass spectroscopy methods of Köster and Monfort the identity of a nucleotide is determined by releasing a releasable mass label during DNA spectroscopy. Thus, Allen’s cantilever method is *not* combinable with the mass spectroscopy methods of Köster and Monfort. As a result, even if a person of ordinary skill in this art would have been motivated to combine Allen with Köster and Monfort, which Applicants respectfully disagree, one would not have arrived at the claimed method of the present invention.

New claims 86-89 are supported by original claim 9. These new claims recite that the mass labels are selected from the group consisting of nanoparticles, nanoparticle aggregates, carbon nanotubes, fullerenes, functionalized fullerenes, functionalized fullerenes, quantum dots, dendrimers, polymers, and combinations thereof. Please note that the releasable mass labels of Köster and Monfort are totally different from the attached mass labels recited in new claims 86-89. In fact, the species of mass labels from original claim 9 that could be used as releasable

mass labels have been excluded in new claims 86-89.

In view of the above amendment, applicant believes the pending application is in condition for allowance.

Dated: November 14, 2007

Respectfully submitted,

By \_\_\_\_\_

Raj S. Davé

Registration No.: 42,465

DARBY & DARBY P.C.

P.O. Box 770

Church Street Station

New York, New York 10008-0770

(212) 527-7700 (Phone)

(212) 527-7701 (Fax)

Attorneys/Agents For Intel Corporation

DRAFT